UNITED STATES PATENT AND TRADEMARK OFFICE

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER OF PATENTS AND TRADEMARKS
Washington, D.C. 20231
www.uspto.gov

APPLICATION NO	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO	CONFIRMATION NO
09/780,205	02/09/2001	Stanislaus Laurens Johan Wouters	4753US	7934

24247 7590 08/30/2002

TRASK BRITT
P.O. BOX 2550
SALT LAKE CITY, UT 84110

EXAMINER
BELYAVSKYI, MICHAIL A

ART UNIT	PAPER NUMBER
1644	10

DATE MAILED: 08/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Application No.	Applicant(s)
09/780,205	WOUTERS ET AL
Examiner	**Art Unit**
Michail A Belyavskyi	1644

Office Action Summary

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *09 February 2001 and 24 June 2002*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-31* is/are pending in the application.

4a) Of the above claim(s) *23,25 and 26* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-22,24 and 27-31* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *09 February 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a)☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1)☒ Notice of References Cited (PTO-892)
2)☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3)☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s). *5*
4)☐ Interview Summary (PTO-413) Paper No(s). _____
5)☐ Notice of Informal Patent Application (PTO-152)
6)☐ Other: _____

DETAILED ACTION

1. Applicant's amendment, filed 6/24/02 (Paper No. 11), is acknowledged.

Claims 1-31 are pending.

Applicant's election of Group I, claims 1, 3-7, 9-12, 13-19, 30 and 31, and Porphyromonas gingivalis as species of a pathogenic micro-organism and F(ab) as species of antibody in Paper No. 11 is acknowledged. Because applicant did not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)). During the phone interview on 08/20/02, Applicant also elected a protease as a species of an enzyme.

In view of Applicant's amendment filed 6/24/02 (Paper No. 11), claims 2, 8, 20, 21, 24 and 27-29 are rejoined with the elected Group I. In order to facilitate the prosecution of this application the prior art search was extended to include claim 22 as it reads on glucose oxidase, as species of oxidase enzyme and *Streptococcus mutans* as species of pathogenic micro-organism recited in Claim 29.

Claims 23 and 25-26 are withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b) as being drawn to nonelected inventions.

Claims 1-22, 24 and 27-31 are under consideration in the instant application.

2. Acknowledgment is made of applicant's claim for foreign priority based on an application filed in August 10, 1998 on Netherlands Application NO: 1009834. It is noted, however, that applicant has not filed a certified copy of the 1009834 application as required by 35 U.S.C. 119(b).

3. The following is a quotation of the second paragraph of 35 U.S.C. 112.

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

4. Claims 1-22 ,24 and 27- 31 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 1 is indefinite and ambiguous in the recitation of "epitope being broken under specifically chosen different conditions" and "lie within physiologically acceptable limits". The characteristics and metes and bounds of "specifically chosen different conditions" and "physiologically acceptable limits" are unclear and indefinite.

5. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same, and shall set forth the best mode contemplated by the inventor of carrying out his invention.

6. Claims 1-22, 24 and 27- 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for an antibody or fragment thereof which binds to an epitope and broken from an epitope under specifically chosen conditions recited in Table 1 does not reasonably provide enablement for an antibody or fragment thereof which binds to en epitope and broken from an epitope under any broadly recited conditions. In addition, claims 4-8, 10 and 12 recites an overlapping ranges of pH (claims 4-8) and ion strength (claim 10 and 12 in particular) at which an antibody or fragment thereof binds to and broken from an epitope. How can mutually exclusive endpoints be achieved at the same pH and ion strength? Simonson et al., (US Patent 4,138,476) teach that the ability of antibody-enzymes complex to be retain in the oral cavity depends on pH and in oral fluids is vary from 5.4 to 7.8 and can be diminished by the tendency for the pH of the oral fluid to rise to the 6.2 to 7.4 range. (see entire document, column 1, lines 55-67 and column 2, lines 5-10 in particular) In addition, Weir ed. (Immunochemistry, Volume 1, 1986, p38.1-38.15 Blackwell Scientific Publication, Oxford) teaches that ability of antibody and fragment thereof to bind to and eluted from an epitope is unpredictable and varies depending on pH and ion strength (see pages 38.5-38.6 in particular). Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use an antibody or fragment thereof which binds to en epitope and broken from an epitope under any broadly recited conditions other than under specifically chosen conditions recited in Table 1.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected to use the invention commensurate in scope with these claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 18 24 (CCPA 1970).

Because of the lack of sufficient guidance and predictability in determining on how to use an antibody or fragments thereof that able to bind to and broken from an epitope under any broadly recited conditions, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

7. Claims1-22, 24 and 27- 31 are rejected under 35 U.S.C. 112, first paragraph, because the specification while being enable for antibody or fragment thereof that binds to a dye and detects the plaque or binds to a diagnostically, therapeutically or cosmetically active substance and suitable for targeting and local administration of active substances for therapeutic treatment of infections in the oral cavity does not reasonable provide enablement for any antibody or fragment thereof which binds to en epitope and broken from an epitope under any broadly recited conditions. Applicant himself acknowledge that the ability of an antibodies to be broken from an epitope at any desired moment can be of benefit only for removing the dye which are used for the detection of dental plaque or other oral pathogens, without lips, tongue and gums remained coloured for a long time (Page 2, lines 19-34 of the specification as filed). The specification as filed does not adequately teach what other benefits of the antibody or fragments thereof that are capable of binding to therapeutically or cosmetically or diagnostically active substance and able to bind to and broken from an epitope u under specifically chosen condition would be.
Moreover, Simonson et al., (US Patent 4,138,476) teach that the longer the antibody-enzyme complex bound to en epitope the better the therapeutic outcome would be (see Abstract in particular). Thus, Applicant has not provided sufficient guidance to enable one skill in the art to use an antibody or fragment thereof which binds to en epitope and broken from an epitope under any broadly recited conditions other than the use of antibody that binds to a dye and detects the plaque or binds to a diagnostically, therapeutically or cosmetically active substance and suitable for targeting and local administration of active substances for therapeutic treatment of infections in the oral cavity.

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected to use the invention commensurate in scope with these claims. The scope of the claims must bear a reasonable correlation with the scope of enablement. See In re Fisher, 166 USPQ 18 24 (CCPA 1970).

Without sufficient guidance how to use an antibody or fragments thereof that are capable of binding to therapeutically or cosmetically or diagnostically active substance and able to bind to and broken from an epitope u under specifically chosen condition, the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue.

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
> *(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.*

9. Claims 1-4, 6-22 and 28 -31 are rejected under 35 U.S.C. 102(b) as being anticipated by Beggs et al., (US Patent NO: 5,490,988) as evidenced by Goding (Monoclonal Antibodies: Principles and Practice, 1983, Academic. Press, New York. see entire book, particularly pages 44-45).

Beggs et al. teach a antibody and antibody fragment, comprising F (ab) or Fv fragments that are able to bind to a target site through antibody –antigen binding (see entire document , column 1, lines 39-41 and column 2, lines 18-20 in particular). Beggs et al., further teach that antibody or antibody fragment is capable of use in a target or temporally diagnostic of externally accessible parts of a human body, particularly bind to an antigenic component of dental plaque under physiologically acceptable limits (see column 4, lines 16-30 in particular). Beggs et al., also teach that the antibody or fragment thereof binds therapeutic active agent, wherein therapeutic agent comprises an enzyme (see column 5, lines 19-42, in particular). The antibody fragment is a fragment of an antibody to *Streptococcus. mutans* and the therapeutic agent is glucose oxidase (column 4, lines 22-27 in particularly). Begges et al., also teach that the antibody or fragment thereof will be used to detect plaque in oral cavity or capable of bleaching teeth (column 4, lines 25-60 in particular). Beggs et al., also teach that antibody and the therapeutic agents are incorporated in one or more pharmaceutically acceptable dilutent or carrier (column 5, lines 44-46 in particular). Beggs et al., also teach composition useful as a teeth cleaning agent, mouthwash, toothpaste comprising antibody or fragment thereof (column 5, lines 65-67 and column 6, lines 1-6 in particular).

Beggs et al. do not explicitly teach that bonds between antibody or fragment thereof and antigen can be broken under specifically chosen conditions.

As is evidenced by Goding (see entire book, pages 44-45 in particular) it is considered to be an inherent properties of all antibody and fragment thereof that the binding to an epitope is reversible and depends on pH and ionic strength. Moreover, during the optimization of each purification protocol for each antibody of interest and a fragment thereof, the parameters such as pH and ionic strength play an essential role and that it is an inherent properties of all antibody and fragment to bind to an epitope under one set of specifically chosen conditions and be eluted from an epitope (bound of antibody to an epitope is broken) under specifically chosen different conditions. (pages 44-45 in particular).

Since the office does not have a laboratory to test the reference antibody or fragment thereof, it is applicant's burden to show that the reference antibody or fragment thereof is different from the antibody or fragment thereof recited in claims 1-4, 6-22 and 28 - 31. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald* et al., 205 USPQ 594 (CCPA 1980).

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> *(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.*

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

Claims 1-22 and 28-31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Beggs et al., (US Patent NO: 5,490,988) in view of Goding (Monoclonal Antibodies: Principles and Practice, 1983, Academic. Press, New York. see entire book, particularly pages 44-45).

The teaching of Beggs et al., has been discussed, supra.

Beggs et al. do not explicitly teach that an antibody or fragment thereof can bind to and be eluted from an epitope at specifically chosen conditions, recited in claims 4-12.

Goding teaches that during optimization of each purification protocol for each antibody of interest and a fragment thereof, the parameters such as pH and ionic strength play an essential role and that it is an inherent properties of all antibody and fragment to bind to an epitope under one set of specifically chosen conditions and be eluted from an epitope (bound of antibody to an epitope is broken) under specifically chosen different conditions. (pages 44-45 in particularly).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to determine all operable and optimal rangers of pH and ion strength at which antibody or fragment thereof binds to and eluted from an epitope, as taught by Goding and use it for antibody or fragment thereof taught by Beggs et al. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because determine optimal rangers of pH and ion strength at which antibody or fragment thereof binds to and eluted from an epitope, as taught by Goding would be beneficial for prolonging the therapeutic effectiveness of therapeutic agents that are delivery to the target site using antibody or fragment thereof, as taught by Begges et al.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

11. Claims 1-4, 6-21, 24, 27, 28 and 30-31 are rejected under 35 U.S.C. 102(b) as being anticipated by Cummins et al .(EP 0736544) as evidenced by Goding (Monoclonal Antibodies: Principles and Practice, 1983, Academic Press, New York, see entire book, particularly pages 44-45).

Cummins et al. teach monoclonal antibody and fragment thereof to salivary pellicle, which are capable of recognizing cryptitopes. These antibody and fragment thereof are particularly suitable to treat oral cavity (see entire document, Abstract in particular). Cummins et al. teach various binding conditions that lie within physiologically acceptable limits, including pH and ion strength (page 4, lines 38-40 in particular). Cummins et al. also teach that antibody and fragment thereof binds diagnostically, therapeutically or cosmetically active substance (see Abstract and pages 3-4 in particular) and can be visualized by using fluorescent labeled antibodies (page 11 in particular). Cummins et al., teach a composition comprising at least one antibody and physiologically acceptable dilutent that is useful as a cleaning agent (see Example 5 in particular) Cummins et al., teach that diagnostically, therapeutically or cosmetically active substance comprises enzyme such as a proteases, including papain, pepsin, trypsin, ficin and bromelin (page 3, lines 35-55 in particular). Cummins et al. teach the antibody or fragment thereof is capable of binding an epitope of a pathogenic micro-organism (page 3, lines 1-5 in particular) and can be used for teeth bleaching (page 3, lines 3-5 in particular).

Cummins et al. do not explicitly teach that bonds between antibody or fragment thereof and antigen can be broken under specifically chosen conditions.

As is evidenced by Goding (see entire book, particularly pages 44-45) it is considered to be an inherent properties of all antibody and fragment thereof that the binding to an epitope is reversible and depends on pH and ionic strength. Moreover, during the optimization of each purification protocol for each antibody of interest and a fragment thereof, the parameters such as pH and ionic strength play an essential role and that it is an inherent properties of all antibody and fragment to bind to an epitope under one set of specifically chosen conditions and be eluted

from an epitope (bound of antibody to an epitope is broken) under specifically chosen different conditions. (pages 44-45 in particularly).

Since the office does not have a laboratory to test the reference antibody or fragment thereof, it is applicant's burden to show that the reference antibody or fragment thereof is different from the antibody or fragment thereof recited in claims 1-4, 6-21, 24, 27 and 28. See *In re Best*, 195 USPQ 430, 433 (CCPA 1977); *In re Marosi*, 218 USPQ 289, 292-293 (Fed. Cir. 1983); *In re Fitzgerald* et al., 205 USPQ 594 (CCPA 1980).

12. Claims 1-4, 6-21, 24, 27, 28 and 30 -31 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cummins et al.,(EP 0736544) in view of Goding (Monoclonal Antibodies: Principles and Practice, 1983, Academic. Press, New York. see entire book, particularly pages 44-45).

The teaching of Cummins et al has been discussed, supra.

Cummins et al., do not explicitly teach that an antibody or fragment thereof can bind to and be eluted from an epitope at specifically chosen conditions, recited in claims 4-12.

Goding teaches that during optimization of each purification protocol for each antibody of interest and a fragment thereof, the parameters such as pH and ionic strength play an essential role and that it is an inherent properties of all antibody and fragment to bind to an epitope under one set of specifically chosen conditions and be eluted from an epitope (bound of antibody to an epitope is broken) under specifically chosen different conditions. (pages 44-45 in particular).

It would have been obvious to one of ordinary skill in the art at the time the invention was made to determine all operable and optimal rangers of pH and ion strength at which antibody or fragment thereof binds to and eluted from an epitope, as taught by Goding and use it for antibody or fragment thereof taught by Cummins et al. Further, it has been held that where the general conditions of a claim are disclosed in the prior art, discovering the optimum or workable ranges involves only routine skill in the art. *In re Aller*, 220 F2d 454,456,105 USPQ 233; 235 (CCPA 1955). see MPEP § 2144.05 part II A.

One of ordinary skill in the art at the time the invention was made would have been motivated to do so, because determine optimal rangers of pH and ion strength at which antibody or fragment thereof binds to and eluted from an epitope, as taught by Goding would be beneficial for prolonging the therapeutic effectiveness of therapeutic agents that are delivery to the target site using antibody or fragment thereof, as taught by Cummins et al.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

13. Claim 29 is rejected under 35 U.S.C. 103(a) as being unpatentable over Beggs et al., (US Patent NO: 5,490,988) in view of Goding (Monoclonal Antibodies: Principles and Practice, 1983, Academic. Press, New York. see entire book, particularly pages 44-45) as applied to claims 1-22 and 28-31 as above, and further in view of Cole et al., (Immunol. &Infect. Diseases 1993, 3, 33-35)

The teachings of Beggs et al., and Goding have been discussed, supra.

The claimed invention differs from the reference teaching only by the recitation of an antibody capable of binding *Porphyromonas gingivalis*.

Cole et al., teach an antibody to *Porphyromonas gingivalis* (see entire document, Abstract in particular). Cole et al., further teach that this antibody play essential role in the immunopathology of periodontal disease.

It would have been obvious to one of ordinary skill in the art at the time the invention was made to apply the teaching of Cole et al., and those of Beggs et al., and substitute antibody capable of binding to one pathogenic micro-organism associated with periodontal disease with antibody capable of binding with another pathogenic micro-organism associated with periodontal disease.

One of ordinary skill in the art at the time the invention was made would have been motivated do so, because antibody to *Porphyromonas gingivalis* are essential in the immunopathology of periodontal disease and could be used to delivery of the therapeutic agents to the target site as taught by Beggs et al.

From the combined teaching of the references, it is apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was *prima facie* obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michail Belyavskyi whose telephone number is (703) 308-4232. The examiner can normally be reached Monday through Friday from 9:00 AM to 5:30 PM. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Michail Belyavskyi, Ph.D.
Patent Examiner
Technology Center 1600
August 26, 2002

CHRISTINA CHAN
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600